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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/957,458	09/21/2001	Yu-Hua Una Chen-Bettecken	P66567US0	2503

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WASHINGTON, DC 20004

EXAMINER

CROUCH, DEBORAH

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 10/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/957,458

Applicant(s)

CHEN-BETTECKEN, YU-HUA UNA

Examiner

Deborah Crouch, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 12, 15 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13, 14 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 September 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/9/01, 5/24/05</u> . | 6) <input type="checkbox"/> Other: _____ |

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Applicant's election of group 1, claims 1-11, 13, 14 and 16 in the reply filed on August 16, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Please note that group I set forth in the restriction/election requirement mailed June 16, 2005 included claims 1-11, 13, 14 and 16. These claims are examined below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13, 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for growing stem cells comprising culturing keratinocyte stem cells with keratinocyte stem cells transformed with a nucleic acid construct comprising a DNA sequence encoding a cytokine in a tetracycline regulated expression system, wherein the stem cells remain undifferentiated and somatic cells transformed with the system, does not reasonably provide enablement for the breadth of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide guidance for externally regulatable interactions between supporters and stem cells. While guidance is provided for the expression of cytokines from tetracycline regulatable promoter, no such guidance is provided for the general category of "substances." In particular no guidance is provide for promoter sequences that are regulated by heat, light, sound, odor, taste, touch and/or

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electromagnetic waves. The specification does teach or otherwise disclose any such promoters.

Further, the specification does not provide guidance on the culturing of embryonic stem cells by the claimed method. At the time of filing, only fibroblasts were known to provide an environment whereby embryonic stem cells did not differentiate. The particular factor or factors supplied by fibroblasts to inhibit differentiation was not known in art nor disclosed by the specification.

The specific examples demonstrate keratinocyte stem cells transfected with a tetracycline regulated expression system where expression of a cytokine gene, IL-3, IL-6 and CNTF prevented the differentiation of keratinocyte stem cells (Examples 1-5). The specific examples (6 and 7) also address the co-culture of fetal lung cells with trachea stems transfected with an IL-3 DNA sequence. However, these examples do not support an inhibition of differentiation because fetal lung cells are differentiated. The specification does not teach that lung stem cells were isolated, and in fact it isn't even clear from the art if such cells can be presently isolated. The specification does not establish the new cell morphology (specification, page 14) is associated with differentiation, that the development of an immature cell to a more mature or terminally differentiated cell. Morphology alone can be an indicator of such because cells change morphology for growth, death and other physiological reasons. There is no disclosure that the lung cells co-cultured with only epithelial stem cells express a different set of markers from those co-cultured with epithelial stem cells transfected with a DNA sequence encoding IL-3.

Thus at the time of the present invention, the skilled artisan would need to engage in an undue amount of experimentation without a reasonable expectation of success to implement the claimed invention for its full breadth.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 9, 11, 14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 are unclear as to the meaning of "spore-like" and the specification does not define the term. All cells are "spore-like" in that all cells have a nucleus.

Claims 1, 11 and 16 are unclear as the phrase "as well as ... expression system" does not state that the subject matter contained therein is being claimed, or if this is a parenthetical statement. Applicant should rewrite the claim to clearly indicate what is being claimed and how it relates to the remainder of the claim.

Claims 1 and 14 are unclear as "molecular and cellular bred" are not terms defined in the specification. It is not clear to what concept the claim refers. Also, "such as" and the inclusion of parenthesis is confusing as to whether or not these elements are being claimed. The claims should be rewritten to eliminate "such as" and parenthesis.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11, 13, 14 and 16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by EP 0753574 A1 (Emerson).

Emerson teaches the co-culture of fibroblasts and hematopoietic stem cells with stem cells transfected with a plasmid having GM-CSF operably linked to a metallothionein promoter

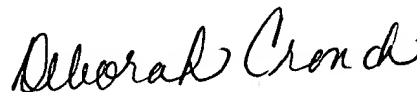
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(col. 2, lines 31-40; col. 9, lines 17-40, lines 49-55; col. 9, line 59 to col. 10, line 2; and col. 10, lines 3-6). Expression of GM-CSF is regulated by the presence of metallothionein in the culture media. The transfected stem cells form a microenvironment for the maintenance of stem cells in an undifferentiated state. NIH 3T3 cells and CV1 cells are a non-stem cell. Thus Emerson clearly anticipates the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Deborah Crouch, Ph.D.
Primary Examiner
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October 21, 2005